

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 17 July 2001 (17.07.01)	
<b>International application No.</b> PCT/US00/40987	<b>Applicant's or agent's file reference</b> FP68294-1DAV
<b>International filing date</b> (day/month/year) 25 September 2000 (25.09.00)	<b>Priority date</b> (day/month/year) 23 September 1999 (23.09.99)
<b>Applicant</b> LUO, Ying et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

21 April 2001 (21.04.01)

☐ in a notice effecting later election filed with the International Bureau on:
2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

H. Zhou

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

BREZNER, David, J.  
Flehr Hohbach Test Albritton &  
Herbert LLP  
Suite 3400  
4 Embarcadero Center  
San Francisco, CA 94111-4187  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

19 July 2001 (19.07.01)

Applicant's or agent's file reference

FP68294-1

RMS/DR

International application No.

PCT/US00/40987

## IMPORTANT NOTIFICATION

International filing date (day/month/year)

25 September 2000 (25.09.00)

1. The following indications appeared on record concerning:



the applicant



the inventor



the agent



the common representative

Name and Address

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:



the person



the name



the address



the nationality



the residence

Name and Address

XU, Xiang  
185 Cymbidium Circle  
South San Francisco, CA 94080  
United States of America

State of Nationality

CN

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

**The person identified in Box 2. has been recorded as additional applicant/inventor for the purposes of the United States of America only.**

4. A copy of this notification has been sent to:



the receiving Office



the International Searching Authority



the International Preliminary Examining Authority



the designated Offices concerned



the elected Offices concerned



other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Margret Fourné-Godbersen

Telephone No.: (41-22) 338.83.38

004162409

# PATENT COOPERATION TREATY

-file-  
-faxed-

**PCT**

From the INTERNATIONAL BUREAU

## NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

To:

BREZNER, David, J.  
Flehr Hohbach Test Albritton &  
Herbert LLP  
Suite 3400  
4 Embarcadero Center  
San Francisco, CA 94111-4187  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)  
29 October 2001 (29.10.01)

Applicant's or agent's file reference  
FP68294-1 *PS 1 200 Rms DHR* ✓

International application No.  
PCT/US00/40987 ✓

### IMPORTANT NOTIFICATION

International filing date (day/month/year)  
25 September 2000 (25.09.00)

1. The following indications appeared on record concerning:

☒ the applicant      ☒ the inventor      ☐ the agent      ☐ the common representative

Name and Address  
HUANG, Betty  
771 Douglas Street  
San Leandro, CA 94577  
United States of America

State of Nationality  
US

State of Residence  
US

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person      ☐ the name      ☐ the address      ☐ the nationality      ☐ the residence

Name and Address  
SEE OBSERVATIONS BELOW.

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

The applicant and inventor identified in Box 1 has been deleted from the record. ✓

4. A copy of this notification has been sent to:

☒ the receiving Office      ☐ the designated Offices concerned  
☐ the International Searching Authority      ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority      ☒ other: HUANG, Betty

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Diana NISSEN

Telephone No.: (41-22) 338.83.38



(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
29 March 2001 (29.03.2001)

PCT

(10) International Publication Number  
**WO 01/21799 A1**

(51) International Patent Classification<sup>7</sup>: C12N 15/12,  
C07K 14/47, 16/18, G01N 33/68

(21) International Application Number: PCT/US00/40987

(22) International Filing Date:  
25 September 2000 (25.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
09/404,010 23 September 1999 (23.09.1999) US

(63) Related by continuation (CON) or continuation-in-part  
(CIP) to earlier application:  
US Not furnished (CIP)  
Filed on Not furnished

(71) Applicant (for all designated States except US): RIGEL  
PHARMACEUTICALS, INC. [US/US]; 240 East Grand  
Avenue, South San Francisco, CA 94080 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): LUO, Ying  
[CN/US]; 32 Chester Circle, Los Altos, CA 94022 (US).  
HUANG, Betty [US/US]; 771 Douglas Drive, San Leandro,  
CA 94577 (US).

(74) Agents: BREZNER, David, J. et al.; Flehr Hobbach Test  
Albritton & Herbert LLP, Suite 3400, 4 Embarcadero Center,  
San Francisco, CA 94111-4187 (US).

(81) Designated States (national): AU, CA, JP, US.

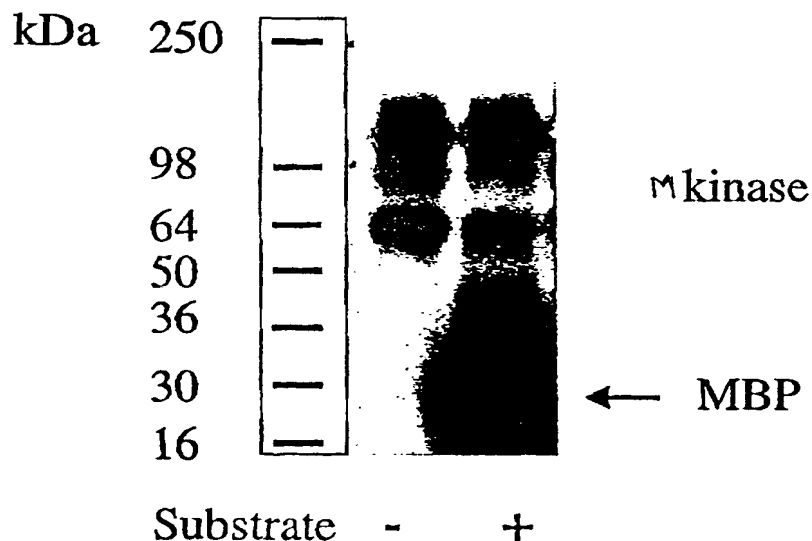
(84) Designated States (regional): European patent (AT, BE,  
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,  
NL, PT, SE).

**Published:**

- With international search report.
- Before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments.

For two-letter codes and other abbreviations, refer to the "Guidance  
Notes on Codes and Abbreviations" appearing at the beginning  
of each regular issue of the PCT Gazette.

(54) Title: TRAF4 ASSOCIATED CELL CYCLE PROTEINS, COMPOSITIONS AND METHODS OF USE



(57) Abstract: The present invention is directed to novel polypeptides, nucleic acids and related molecules which have an effect on or are related to the cell cycle. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Further provided by the present invention are methods for identifying novel compositions which mediate cell cycle bioactivity, and the use of such compositions in diagnosis and treatment of disease.



WO 01/21799 A1

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>FP68294-1DAV</b>	<b>FOR FURTHER ACTION</b> <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/US 00/ 40987</b>	International filing date (day/month/year) <b>25/09/2000</b>	(Earliest) Priority Date (day/month/year) <b>23/09/1999</b>
Applicant <b>RIGEL PHARMACEUTICALS, INC.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.  
☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**TRAF4 ASSOCIATED CELL CYCLE PROTEINS, COMPOSITIONS AND METHODS OF USE**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

4

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐

None of the figures.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box I.2

Claims Nos.: 15

Claim 15 relating to binding polypeptides to the polypeptide of claim 15 could not be searched as its subject-matter was insufficiently disclosed .

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## PCT INTERNATIONAL COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTICE INFORMING THE APPLICANT OF THE  
COMMUNICATION OF THE INTERNATIONAL  
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

BREZNER, David, J.  
Flehr Hohbach Test Albritton &  
Herbert LLP  
Suite 3400  
4 Embarcadero Center  
San Francisco, CA 94111-4187  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

29 March 2001 (29.03.01)

Applicant's or agent's file reference

FP68294-1 ~~DAF~~ ~~DD~~ ~~DRms~~ ~~DHR~~ ~~32~~

## IMPORTANT NOTICE

International application No.

PCT/US00/40987 ✓

International filing date (day/month/year)

25 September 2000 (25.09.00) ✓

Priority date (day/month/year)

23 September 1999 (23.09.99) ✓

Applicant

RIGEL PHARMACEUTICALS, INC. et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:

AU,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

CA,EP,JP

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 29 March 2001 (29.03.01) under No. WO 01/21799

**REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)**

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a **demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

**REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))**

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

J. Zahra

Telephone No. (41-22) 338.83.38

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/40987

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 C12N15/12 C07K14/47 C07K16/18 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, MEDLINE, BIOTECHNOLOGY ABS, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 05175 A (MATOSSIAN ROGERS ARPI) 4 February 1999 (1999-02-04) -- abstract; claims 1-29; figure 7 ---	1,6-11, 19
X	US 5 645 999 A (KOFF ANDREW C ET AL) 8 July 1997 (1997-07-08) abstract; claims 1-8 ---	19,22,23
X	WO 97 07134 A (GENENTECH INC ;TULARIK INC (US)) 27 February 1997 (1997-02-27) abstract; claims 1-38; figure 2 / --- -/--	19,22,23

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*8\* document member of the same patent family

Date of the actual completion of the international search

14 February 2001

Date of mailing of the international search report

27/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel (+31-70) 340-2040. Tx 31 651 epo nl.  
 Fax: (+31-70) 340-3016

Authorized officer

Gurdjian, D

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/40987

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KRAJEWSKA MARYLA ET AL: "TRAF-4 expression in epithelial progenitor cells. Analysis in normal adult, fetal, and tumor tissues." AMERICAN JOURNAL OF PATHOLOGY, vol. 152, no. 6, June 1998 (1998-06), pages 1549-1561, XP000982100 ISSN: 0002-9440 the whole document	20,21
Y	BIECHE VVAN CATHERINE TOMASETTO ET AL: "Two distinct amplified regions at 17q11-q21 involved in human primary breast cancer." CANCER RESEARCH, vol. 56, no. 17, 1996, pages 3886-3890, XP002160267 ISSN: 0008-5472 abstract	20,21
Y	REGNIER CATHERINE H ET AL: "Presence of a New Conserved Domain in CART1, a Novel Member of the Tumor Necrosis Factor Receptor-associated Protein Family, Which Is Expressed in Breast Carcinoma." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 43, 1995, pages 25715-25721, XP002160268 ISSN: 0021-9258 abstract	20,21
A	LETWIN K ET AL: "A MAMMALIAN DUAL SPECIFICITY PROTEIN KINASE NEK1 IS RELATED TO THE NIMA CELL CYCLE REGULATOR AND HIGHLY EXPRESSED IN MEIOTIC GERM CELLS" EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 11, no. 10, 1992, pages 3521-3531, XP002160269 ISSN: 0261-4189 cited in the application abstract; figures 1,2	1-14
P,X	WO 00 26670 A (BOEHRINGER INGELHEIM PHARMA) 11 May 2000 (2000-05-11) the whole document	19-23

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 15

Claim 15 relating to binding polypeptides to the polypeptide of claim 15 could not be searched as its subject-matter was insufficiently disclosed .

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PT/US 00/40987

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9905175	A	04-02-1999	GB 2327423 A	27-01-1999
			AU 8451798 A	16-02-1999
			BR 9810118 A	08-08-2000
			CN 1264426 T	23-08-2000
			EP 0998556 A	10-05-2000
			PL 338449 A	06-11-2000
<hr/>				
US 5645999	A	08-07-1997	US 5449755 A	12-09-1995
			US 5861259 A	19-01-1999
			US 5807698 A	15-09-1998
			US 5783661 A	21-07-1998
			AU 676137 B	06-03-1997
			AU 2666392 A	27-04-1993
			CA 2119443 A	01-04-1993
			EP 0604560 A	06-07-1994
			JP 7502164 T	09-03-1995
			WO 9306123 A	01-04-1993
<hr/>				
WO 9707134	A	27-02-1997	AU 709535 B	02-09-1999
			AU 6723796 A	12-03-1997
			CA 2227174 A	27-02-1997
			EP 0845005 A	03-06-1998
			JP 11511967 T	19-10-1999
			NZ 315514 A	23-12-1998
			US 6004553 A	21-12-1999
			US 6063585 A	16-05-2000
			US 5789550 A	04-08-1998
<hr/>				
WO 0026670	A	, 11-05-2000	US 6143507 A	07-11-2000